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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/622,719	10/18/2000	Hubert Loewenheim	24356	1261

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EXAMINER	
LACOURCIERE, KAREN A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 07/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/622,719	LOEWENHEIM, HUBERT	
	Examiner	Art Unit	
	Karen A. Lacourciere	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28,31 and 63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28, 31 and 63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 06-14-2004 has been entered.

Claim Rejections - 35 USC § 112

The rejection of record under 35 USC 112, first paragraph, as lacking enablement, has been withdrawn in response to Applicant's claim amendments and arguments presented, along with the data provided in the declaration under 37 CFR 1.132 filed 06-14-2004, which demonstrates an improvement in hearing loss that correlates with a decrease in $p27^{kip1}$ activity.

Claims 28, 31 and 63 are maintained as rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 28, 31 and 63 are drawn to methods that require antisense molecules targeted to generally any mammalian $p27^{kip1}$. The specification does not disclose the

structure (i.e. nucleotide sequence) of any antisense molecules targeted to mammalian $p27^{kip1}$, nor does it disclose the target sequence for any mammalian $p27^{kip1}$, or the common structural elements (e.g. regions of homology) for mammalian $p27^{kip1}$. The prior art at the time of the invention provided 2 antisense molecules targeted to one species of mammalian $p27^{kip1}$ (human $p27^{kip1}$) and disclosed the nucleotide sequence encoding three species of mammalian $p27^{kip1}$.

Claims 28, 31 and 63 are directed to encompass methods that require antisense that hybridizes to and inhibits generally any mammalian $p27^{kip1}$ mRNA, including mammalian species of $p27^{kip1}$ which were not described in the prior art or the specification. The genus of mammalian $p27^{kip1}$ is broad and the species encompassed in the genus is highly variant (for example, with regard to nucleotide sequence) and, therefore, the structure (i.e. nucleotide sequence) of antisense molecules targeting this genus is highly variant. The broad genus of mammalin $p27^{kip1}$ antisense required to practice the claimed methods do not meet the written description provision of 35 USC 112, first paragraph, because none of the species encompassed by the genus were described in the specification and a sufficient number of species to represent the genus were not described in the prior art. Two antisense molecules targeted to one species of $p27^{kip1}$ would not be representative of the broad, highly variant genus claimed, nor would three species of target gene be representative of the genus of mammalian $p27^{kip1}$ genes targeted by antisense and, therefore, the sequence of target genes from which antisense sequences may be derived were not even described in the art at the time of

filing. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of the antisense sequences described in the prior art, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to

> recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.
>
> The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

Therefore, only the two antisense sequences disclosed in the prior art (Hauser et al. (Cell Growth and Differentiation, Vol. 8, Feb 1997, p 203-211) of record), but not the full breadth of the claim, meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed in the prior art are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Response to Arguments

Applicant's arguments filed 06-14-2004 have been fully considered but they are not persuasive. In response to the rejection of record under 35 USC 112, first paragraph for lack of adequate written description, Applicant argues that the amended claims are

adequately described. Applicant's arguments have been considered to the extent that they apply to the rejection under 35 USC 112, first paragraph, set forth herein.

Applicant argues that the sequences of mammalian $p27^{kip1}$ genes are highly related and points to Polyak et al. to support the assertion and states that an alignment of the nucleotide sequences presents an 85% identity for three species (human, mink and mouse). Applicant argues Coates et al. and Hauser et al. disclose antisense inhibitors and one of those antisense molecules (disclosed in both Coates et al. and Hauser et al.) is directed to a region identical in the three known species of $p27^{kip1}$ and that this antisense and another antisense molecule targeting a common region of the three known mammalian $p27^{kip1}$ have been shown to actively effective in inhibiting the expression of $p27^{kip1}$ and, therefore, the skilled artisan would recognize that the inventors were in possession of the invention at the time of the invention.

These arguments have not been found to be persuasive because the genus of antisense molecules targeted to mammalian $p27^{kip1}$ required to practice the scope of the claimed methods is not represented by two antisense sequences, both directed to human $p27^{kip1}$. The two antisense molecules described in the prior art, directed to human $p27^{kip1}$, may inhibit the expression of $p27^{kip1}$ in three other species of mammal, as discussed in Applicant's arguments, however, four species is not representative of the broad genus of mammalian $p27^{kip1}$ encompassed in the claims. Although there are regions of homology between the human gene and two other mammalian species of $p27^{kip1}$, Applicant did not describe this homology, such that the skilled artisan would have been apprised of the common elements of the genus of antisense required by the

claims and, further, three species is not representative of the broad genus of mammalian $p27^{kip1}$ genes targeted in the claimed methods and the broad genus of antisense required to practice the claimed methods.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Lacourciere whose telephone number is (571) 272-0759. The examiner can normally be reached on Monday-Thursday 7:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Lacourciere

KAREN A. LACOURCIERE, PH.D
PRIMARY EXAMINER

Karen A. Lacourciere
June 30, 2004